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Menopausal and Post-Menopausal Conditions in Women.*

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The menopause is a very definite epoch in the life of a woman with which there is nothing comparable in the life of a man. Whilst it is determined by strictly physiological processes these may easily pass on to the pathological, and the physiological readjustments which take place may bring to light hitherto unrecognized and unnoticed dysfunctions in the different organs and systems in the body.

For an understanding of these pathological states it is necesary to have as clear an idea as possible as to what the menopause is, how it is brought about, and what are its normal effects on the various tissues, organs and systems of the body.

The Normal Menopause.

The menopause is the time at which the female reproductive organs cease to function. This cessation of function is directly due to the exhaustion of the primordial follicles in the ovaries so that ovulation no longer takes place and conception is impossible. At the same time the internal secretion of the ovaries fails and menstruation ceases. There then takes place a slow, atrophic change in all the organs of generation, internal and external.

The withdrawal of the ovarian secretion from the circulation causes a temporary upset in the function of other glands of internal secretion such as the thyroid, suprarenals and pituitary. This upset may be evidenced by tissue changes and general symptoms of various kinds and these may be so marked as to constitute a pathological state. It may, however, be stated at the outset that in the average woman with healthy organs the menopause causes very little general upset and is not accompanied or followed by any pathological lesions of the pelvic organs.

In considering the pathological menopause, and disabilities arising from it, it will be well to take up separately the local pelvic lesions, and then disturbances in other organs and systems.

Menopausal Hemorrhage.

The actual cessation of menstruation may take place in a variety of ways. It may occur suddenly and completely without any warning. This is unusual except in those cases where the menopause has been induced artifically by removal of the ovaries at operation or by X-ray radium treatment.

More often the periods first of all become irregular the patient skipping one from time to time, and losing less and less blood at each. The intervals between the periods gradually lengthen until complete cessation occurs. In other instances the amount of the flow may be increased and the periods be more frequent than normal. These conditions may obtain for several months

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or even years before menstruation completely stops. In some such cases the flow becomes very excessive so that it amounts to flooding and the patient may be reduced to an extreme degree of anemia.

It is important to recognize these different ways in which the cessation of menstruation may occur in order to distinguish the physiological from the pathological.

As has been stated cessation of the periodic menstrual flow is due to the withdrawal of the internal secretion of the ovary from the circulation. This withdrawal is as a rule a gradual process and whilst it is occurring certain changes of the nature of a senile atrophy are taking place in the uterus, both in its muscular wall and in its mucous membrane. In the uterine wall there is a gradual replacement of muscle fibre by fibrous and elastic tissue and in the mucous membrane the stroma becomes more fibrous, the blood vessels become fibrosed and the glands atrophy. The endometrium becomes more and more like any other mucous membrane in the body. As the stimulus from the ovarian secretion becomes less strong so the response of this fibrosing uterine mucous membrane becomes more and more feeble. There are fewer active proliferative tissue changes in the premenstrual period, less congestion and, therefore, less loss of blood at the period, and more feeble regenerative changes in the postmenstrual period. The endometrium thus becomes more and more a fixed passive tissue and ultimately so fibrosed as to be incapable of any response to the ovarian hormone.

The smooth, well-ordered menopause, with gradual cessation of menstruation is dependent upon the diminution in the amount of ovarian hormone and the fibrotic changes in the uterus occurring simultaneously and in equal degree.

If the ovarian secretion fails abruptly there will be a sudden and complete cessation of menstruation although the uterus has undergone little or no atrophic change.

On the other hand if the fibrotic changes of the uterus are in advance of the degenerative changes in the ovaries the patient will almost certainly suffer from menorrhagia which may amount to flooding. The reason for this is that the ovarian secretion is still powerful enough to call forth the histological changes in the uterine mucous membrane which culminate in the menstrual flow. That flow is excessive and prolonged, firstly, because the uterine muscle, partly replaced by fibrous tissue, is no longer capable of normal contraction and, secondly, because capillaries in the endometrium have become thickened and sclerosed and are no longer capable of closing by collapse of their walls as they normally should. There is thus both an excessive blood loss and prolongation of the period. This, I think, is the most rational explanation of the excessive menstruation which not infrequently antedates the menopause and also of these cases of profuse hemorrhage occuring in women in the late thirties and early forties.

In these latter there are usually other clinical evidences of premature fibrosis uteri such as lacerated and infected cervix, large, hard, heavy tender uterus, and occasionally inflamed appendages. The cases of severe premenopausal and menopausal hemorrhage due to early and excessive uterine fibrosis do not respond to any form of medical treatment. The uterine wall is incapable of any reaction to such drugs as ergot or pituitary extract. Curettage while necessary for diagnosis is not curative so that if the menorrhagia is severe resort must be had to radiotherapy or hysterectomy. In the choice between these forms of treatment some regard must be had to the possible etiology of the condition. Some of the cases show undoubted evidence of chronic infection with lacerated, eroded and thickened cervices as well as enlargement and

sclerosis of the body. In such the patients present a picture of a chronic toxemia in addition to that of anemia and, in my experience, a total hysterectomy gives them the best hope of good health in the future. On the other hand, we may find the cervix healthy and the only disability of the patient that due to blood loss. In such radium or X-ray treatment is better—always, of course, preceded by a diagnostic curettage.

I believe that a big field of preventive medicine is open to obstetricians and gynecologists in the early recognition and treatment of cervical tears and infections following childbirth as a prophylactic against the development of chronic metritis or fibrosis uteri with its attendant menorrhagia in the later years of sexual life.

There is another histological picture found in some cases of severe menopausal hemorrhage, namely, what we have come to call a cystic glandular hyperplasia of the endometrium. In this condition the endometrium is thickened, the stroma is of normal structure, the blood vessels are large and numerous, but not thickened, and the glands are irregular in size and shape, many of them large and dilated and all with active epithelium. This condition while most commonly seen near the time of the menopause may occur in quite young women. Like fibrosis it is not amenable to drug treatment or curettage and may call for radiotherapy or hysterectomy.

The constant problem that presents itself to us in all these cases of excessive and of irregular bleeding at or near the age of the menopause is that of determining whether the bleeding is really menstrual in origin or whether it may be a symptom of a new growth and especially of a cancer of the cervix or body of the uterus.

It goes without saying that every patient presenting herself to us with these symptoms should have a most careful and complete pelvic and general physical examination. This is sufficient to exclude gross cancer of the vagina and the portio vaginalis of the cervix. It tells us nothing of the upper reaches of the cervical canal or of the endometrium. Information regarding these can be got only by a dilatation of the cervix and curettage of the uterus followed by histological examination of the tissue removed.

Under what circumstances is it our duty to recommend and urge this? In what instances may it safely be dispensed with?

It is necessary to formulate some sort of answer otherwise we should on the other hand miss some early cases of cancer or, on the other, subject needlessly a very large number of women to surgery. In general terms it may be stated that if the bleeding is periodic, lasts only a certain definite number of days and then stops, is preceded and accompanied by the feelings the patient has learned to associate with menstruation, then no matter how excessive it may be it is menstrual in character. Such bleeding is not caused by carcinoma of the endometrium. It may be caused by a fibroid tumor, by a fibrous polyp, by a fibrosis uteri, or by a cyctic glandular hyperplasia. In these cases the amount of blood loss and its effect upon the patient will be the determining factor for or against diagnostic curettage and further surgical or radiological treatment.

Again, if a woman has apparently had the menopause established after a period of irregularity and then four, six, or eight months later again has vaginal bleeding a careful pelvic examination must be made. If such examination reveals nothing abnormal in cervix or vagina we are justified in waiting a short time before urging a curettage. If the bleeding stops in a few days and there is no recurrence we can conclude that it is a belated menstruation. On the other hand if it continues for over a week or stops in a few days and then recurs, no matter how slightly, diagnostic curettage ought to be urged.

If uterine bleeding of any character occurs more than a year after the menopause and nothing can be found on ordinary pelvic examination to account for it we fail in our duty to our patient if we do not advise exploration of the uterus. In this connection let me urge that even when an apparent explanation for the bleeding is found, such as a small cervical mucous polypus, it be not concluded that that is the only cause of the bleeding. I have seen in consultation two patients who had such polpi removed by their doctors in their offices, who continued to bleed, and who both turned out to have carcinoma of the endometrium. I make it a rule when a women past the menopause has vaginal bleeding and a cervical polpy is found that she be given an anesthetic, and the uterus be curetted when the polyp is removed.

If we remember the simple fact that cancer of the uterine endometrium or of the cervix bleeds because it ulcerates and that, therefore, the bleeding is independent of, and unrelated to, menstruation we shall be in less hesiancy as to the type of case in which exploration of the uterus is obligatory. In a case of advanced fibrosis uteri with actively functioning ovaries there is practically continuous bleeding because the blood vessels of the endometrium opened up as the result of one menstrual stimulus have not closed before the next stimulus arrives. In such a case a diagnostic curettage is the only means of distinguishing it from carcinoma or other uterine lesion.

A fibrous polypus projecting from the cervix and ulcerating causes intermittent or continuous bleeding, and such polpi are most often found in women at or after the menopause. The atrophy of the uterus in the postmenopausal period is a factor in extruding such tumors from the uterine wall and out through the cervical canal. It is interesting to note that very often such tumors are found in women who have had several children —the type of patient in whom one least expects to find the ordinary fibroid during active sexual life.

The only other bleeding condition to be mentioned now is senile endometritis, a condition occuring some years after the menopause in a uterus which has undergone extreme atrophy and in which, as a rule, the cervical canal is occluded by plastic adhesions. This occlusion of the cervix is not permanent or complete for it, apparently, allows access to the uterine cavity of organisms of decomposition which acting on the necrosing lining of the uterus produce an extremely fetid discharge. This may escape into the vagina from time to time and in nearly all cases it is blood stained as a result of deep ulceration into the uterine wall. The occurrence of such a fetid blood-stained discharge in a woman past the menopause, of course, at once conjures up the picture of cancer. It is only on diagnostic curettage that that diagnosis can be excluded. In case of so-called menopausal or post-menopausal arthritis the possibility of partial occlusion of the cervix and the locking up of small pockets of pus in the canal or in the uterine cavity should be borne in mind. There are numbers of cases on record where the draining of such collections has resulted in a disappearance of the joint condition.

Leaving now the uterine hemorrhages let us turn for a moment to other conditions arising as a result of the atrophic changes following the menopause. Of these, by far the commonest is cystocele. If the proper supporting fascia of the bladder has been grossly injured during childbirth a cystocele will develop very soon after. Such a cystocele tends to become progressively larger up to and after the time of the menopause. In many instances, however, the damage has not been sufficient to result in a definite prolapse of the bladder at the time and this may not become apparent until one or two years after the menopause when it gradually develops as the result of loss of support

due to atrophy of the pelvic fascia. In such cases incontinence of urine, an inability to retain urine under such strains as coughing, laughing, or making a sudden movement, is a common symptom. As a rule cystocele and prolapse of the other pelvic organs become aggravated after the menopause. It is, therefore, well to advise patients with these conditions to have them treated operatively as soon as their child bearing period is over and certainly before post-menopausal atrophy has rendered the proper fascial and muscular supports of the organs feeble and difficult to define.

I never operate on a case of prolapse in a woman over fifty without thinking of all the years of disability she has gone through, putting off the evil day of operation in the hope that the change of life would make things better and finding instead that it made them worse.

Normally after the menopause the folds of the vagina become smoothed out, the epithelium becomes thin and the walls contract, especially in the region of the fornices which become shallower and shallower until the roof of the vagina becomes cone-shaped with the small atrophied cervix at its apex. At this stage the uterus has become a shrunken organ and as a rule lies in a position of slight retroversion. At this time a condition known as senile vaginitis may develop. This takes the form of small areas from which the epithelium has become completely desquamated and which exude a watery discharge, often blood stained. These areas have a red color giving to the vaginal walls a red, irregularly mottled appearance. Saprophytic organisms grow on the desquamated epithelium producing a thick, often fetid, discharge, which irritates the lower reaches of the canal and the region of the vestibule and vaginal introitus. The patient suffers from itching and pain and may be rendered extremely miserable. There is a tendency for the walls of the vagina to become adherent especially at the roof and dyspareunia may be a prominent symptom. As the result of atrophy in the vestibule there may be undue exposure of the urethral mucous membrane which becomes inflamed and sensitive. Or, a urethral caruncle may develop.

The early stages of this condition of senile vaginitis may be present before the menopause is established. It is important to recognize them then, as treatment may be effective. The application of iodine or of 15 per cent. nitrate of silver solution to the individual areas together with the administration of ovarian substance may be curative. When the discharge is fetid and blood stained no treatment should be undertaken until a possible carcinoma of cervix or fundus uteri has been ruled out.

An extensive atrophic condition may develop in the vestibule, in the labia minora, and round the vaginal entrance. The epidermis becomes thin and the sub-dermic tissue undergoes extreme fibrosis and contracture. There is a severe pruritis and pain from the contraction of the parts. To this condition the name kraurosis has been given. It is extremely resistant to treatment although good results have been recorded in a few cases from the use of ovarian extracts. It is a condition to be distinguished from leukoplakia vulvae which affects the skin surfaces outside the region of the vestibule and which is often a precursor of cancer. Kraurosis is not a precancerous condition except in so far as the severe itching may lead to the production of abrasions and fissures by scratching. Such areas in elderly people are never free from danger.

Pruritis Vulvae is a generic term applied when any condition produces itching in the vulvar and perineal region. It is commoner at the time of and after the menopause than at any other period of life. It always calls for the most careful investigation as it may be due to such a variety of

conditions — pediculi, round worms, glycosuria, irritating cervical and vaginal discharge, leucoplakia, kraurosis and cancer. In some cases all of these can be ruled out and no lesion is detectable except that due to scratching. In such, treatment by X-ray often gives relief. A few words may be said regarding the effect of the menopause on pelvic neoplasms.

Uterine Fibromyoma.

It is a well recognized clinical fact that a woman with uterine fibroids tends to have a delayed menopause. Such women often go on menstruating till well over fifty. It is, therefore, a mistake to encourage a woman who is having menorrhagia from a fibroid tumor to wait for the menopause for relief. She may be incapaciated for the best years of her life if she does so. While small, symptomless fibroids usually undergo retrogression and may practically disappear after the menopause, those which give rise to symptoms of any kind ought to be treated by operation or by radiation whenever these symptoms call for it. At and after the menopause various degenerative changes may occur in the tumors and may make their removal advisable. One of the commonest of these is calcification, which may render the tumor so heavy as to cause pressure symptoms necessitating operation. Reference has already been made to the extrusion of a fibrous polypus at or after the time of the menopause.

Cancer of the Uterus.

One of the very interesting facts regarding the age incidence of cancer is that cancer of the cervix occurs at an earlier age than cancer of the body of the uterus. The former is common at about the age of menopause— thirty-eight to fifty. The latter is common in the years which succeed the menopause —fifty to seventy.

Ovarian Tumors

Ovarian tumors may be present at any age. Those seen in very young girls and those seen in women after the menopause are more likely to be malignant than those occuring in women during their active sexual life. An ovarian tumor in a woman of fifty or over, especially if associated with ascites, should always be regarded with the greatest suspicion.

Let us now turn for a short time to a consideration of the normal changes and the possible disabilities which may occur in the woman generally, at and after, the menopause. These result from the withdrawal of the ovarian hormone from the circulation. I shall not dwell long on this part of the subject.

While it is true that the ovary is essential for reproduction and its internal secretion is necessary for the function of menstruation and for the maintenance of the uterus in such a condition that it can embed and nourish a fertilized ovum yet the ovary in its turn is dependent on other organs for its efficiency. The more the actions of the various ductless glands are investigated the more apparent does it become that there are various and complicated interactions between them and that the failure of one will lead to disordered action in the others. Thus while the menopause is directly due to the failure of the ovary to produce and pass into the circulation its hormone or hormones this failure may be the result of dysfunction of one of the other ductless glands. Thus a thyroid or a pituitary deficiency may lead to amenorrhea and to sterility long before the usual age of the normal menopause. We see this in the case of the thyroid in myxedema and in the case of the pituitary in Froehlichs dystrophia adiposo-genitalis.

So conversely, when the ovarian secretion fails there are effects on the other ductless glands and these effects may produce symptoms. In the normal natural menopause the withdrawal of the ovarian secretion is a slow, gradual process and the adjustments take place with little disturbance to the indivi-

dual. If, however, the ovarian secretion is withdrawn suddenly at the time of the natural menopause or as the result of castration, either by operative removal of the organs or by radiation, marked general disturbance may result. In this connection it is interesting to note that the symptoms of the artificial menopause are always more marked and more prolonged after the removal of comparatively healthy ovaries than after the removal of those more grossly diseased. In the latter case there has been a gradual failure of function and readjustments have been going on before the final ablation.

I heard from a colleague the other day of a patient who had a castration dose of X-ray fifteen years ago to render her sterile and who now at the age of forty-five suffers from menopausal symptoms as intensely as she did a year after treatment.

Most women have an altogether exaggerated and distorted idea of the disabilities and dangers of the menopause. This is due to that unfortunate trait in the character of the average woman which impels her to communicate to her kind all the stories of distress and disaster which may have come to her notice and to let nothing be lost in the telling thereof. It has always seemed to me strange that such tales should be so common regarding natural processes like childbirth and the menopause and that an educational campaign should be necessary to instill a little knowledge regarding the early symptoms and nature of cancer.

In the average healthy woman the menopause is not accompanied by distressing symptoms and it is not likely to precipitate disease in extra-genital organs. She may experience certain vasomotor disturbances such as hot flushes and sudden perspirations, slight attacks of dizziness or of headache. These are the result of imperfect vasomotor control as the result of the gradual withdrawal of the ovarian secretion. Such symptoms are usually more marked with an artificial menopause due to castration than with a normal climacteric. They are best relieved, in my experience, by the administration of a preparation of Whole Ovarian Gland. I know that it is held by many, and they have some scientific evidence for their belief, that the oral administration of all gland preparations except thyroid is valueless, as their substances are not absorbed through stomach or intestine. I have no proof to the contrary, but I have frequently noted clinical improvement in patients with the above mentioned symptoms when ovarian substance has been given by mouth. When both ovaries have been removed by operation the implantation of even a thin slice of one of them into the rectus muscle postpones and may ward off altogether these unpleasant symptoms.

General nervous symptoms, of which the commonest are irritability, inability to concentrate, and mental depression, occur in a certain number of women. These symptoms are the same as those which many women experience during and towards the end of each menstrual period. It has been conclusively proved that "in the organism of the healthiest woman there is a monthly period of depression in her vital processes which finds definite expression in all her activities," including the psychic and nervous (Goraves). When the monthly cycle is disappearing at the menopause this period of depression may become more prolonged and may last for weeks or months instead of days. If there is an inherent or instability of the nervous system all the symptoms will be more marked. They are aggravated by dwelling upon them and by the fact that at this time many women are leading an aimless and purposeless life. Their children have grown up and have homes of their own. Their households no longer demand the greater part of their day. They have no mental occupation and fall an easy prey to depression and ennui. As Brettauer lately pointed out, if more women cultivated a hobby which would

occupy and interest them after their retirement from the active business of rearing a family and managing a household there would be fewer psychoneurotics.

One might mention a host of other pathological conditions occurring in women at or after the age of the menopause, but these would be outside the scope of our subject, for they are in no way related to the menopause as such, but are incident to the aging process.

For most women fortunately the years which succeed the menopause are the most peaceful, the most mentally productive, and the most satisfactory in their lives.

Banti's Disease. *

By E. H. BENSLEY, B.A., 3T0, and J. E. GUNDY, 2T9.

Symptomatology.

The symptomatology of Banti's disease can be divided into three stages:

1. The pre-ascitic stage lasting 3 to 5 years and characterized by splenomegaly and secondary anaemia.

The onset is insidious. There is a gradually increasing weakness, fatigability, and pallor. A common complaint is that of "feeling tired on getting up in the morning." Next the patient begins to suffer from digestive disturbances, abdominal discomfort, and pain which may draw his attention to the enlargement of the spleen. A large percentage of cases suffer from hematemesis while a smaller number complain of diarrhoea and passing bright red blood in the stools.

On physical examination the patient is found to be a pale individual of the adolescent or young adult period of life. The large, firm, smooth spleen, not uncommonly reaching to the level of the umbilicus is easily palpated and is often tender. A mild temporary ascites is sometimes present following attacks of abdominal pain. There may be occasional bouts of slight fever. The blood picture is that of a moderately severe secondary anaemia. The number of red blood cells is diminished — the count ranging from about 2,500,000 to normal. The percentage of haemoglobin is markedly decreased and the colour index is therefore low. Leukopenia is an almost constant finding. The low white blood count is due largely to a reduction of neutrophilic leucocytes, so that there is a relative lymphocytosis. If the white blood count is above normal one suspects that this must be a more or less transient rise caused by some extraneous factor such as an infection. A study of the platelets in Banti's disease is extremely interesting. Rosenthal divides the disease into two groups—(i) those cases in which the blood platelets are definitely diminished and (ii) cases in which the platelets are not definitely decreased but are normal or almost normal in number. Of 9 cases critically studied by him 5 fell into the first group with low platelet counts and 4 into the second. Those in the first group all showed haemorrhagic tendencies, while one of them had symptoms of purpura haemorrhagica.

2nd Stage—

The intermediate stage of the disease lasts for several months and is characterized by enlargement of the liver and the passing of scanty highly coloured urine containing an excess of urobilin. The indirect Van den Bergh reaction is positive.

3rd Stage—

The final stage is of 1—2 years duration. In it the patient develops all the signs and symptoms of portal cirrhosis of the liver. Added to the patient's other symptoms then we have a recurrent painless ascites and occasional slight jaundice.

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*Continued from March number.

Let us consider the underlying factors in the production of some of these symptoms.

(1) Firstly, the weakness, fatigue, and pallor are of course attributable to the secondary anaemia.

There are three possible factors contributing to the development of this anaemia—(a) depression of the bone marrow as evidenced by a decrease in red blood cells, platelets, and granulocytes, and by a lack of reticulocytes, (b) loss of blood by haemorrhage from the stomach or large bowel, and (c) possibly an increased destruction of red blood cells.

(2) Hematemesis . The haemorrhage is either from the gastric mucosa or from aesophageal varices. In any case the explanation is the same and the cause is possibly twofold — (a) thrombocytopenia, and (b) congestion of the veins in the wall of the stomach due to thrombosis in the splenic vein.

(3) The passing of bright red blood in the stools is explained in a similar manner, the thrombosis in this case occurring in the inferior mesentric vein.

(4) Gastric disturbances are due in part at least to the congestion in the mucosa of the stomach and possibly also to congestion in the pancreas.

(5) Abdominal discomfort is explained by the presence of the enlarged heavy spleen.

(6) Abdominal pain may be of two origins.

(i) Due to perisplenitis, evidences of which are frequently found at operation and at autopsy. This pain may be referred to left thoracic and abdominal walls in the area supplied by the last 6 thoracic nerves. It is commonly referred however to the left shoulder region. It is increased on deep breathing and is often accompanied by an audible friction rub.

(ii) Another cause of abdominal pain may be thrombosis in the splenic, inferior mesenteric, or superior mesenteric veins.

Diagnosis.

The diagnosis is made on.

1. The history of a gradual onset of weakness and anaemia and in a large percentage of cases — hematemesis. Chronicity is a point to be considered in the diagnosis.

2. The presence of a considerably enlarged spleen.

3. The haematological findings—
   - A moderately low red blood count.
   - A low percentage of IIb.
   - A low colour index.
   - A leukopenia with relative lymphocytosis.
   - Thrombocytopenia.

4. The absence of any known aetiology such as syphilis or malaria.

Differential Diagnosis.

Banti's disease must be differentiated from other anaemias associated with splenomegaly. Certain pathological conditions often designated pseudo-Banti's disease, present such similar pictures that differentiation during life is difficult or even impossible. Persistence of the umbilical vein is an example of this. It is, however, a very rare anomaly and can probably be disregarded in the diagnosis.

Gaucher's disease of the spleen is also very rare—only about 12 cases having been reported in the literature in the last decade. It is markedly chronic. An average case will progress for twenty years. The signs and symptoms resemble closely those of Banti's disease and the differentiation is usually made at autopsy.

Syphilis of the Liver and Spleen.—Osler described four cases of syphilitic cirrhosis, two of them congenital, with enlarged spleen, secondary anaemia and hematemesis. It is well known that syphilis may give a picture exactly like that of Banti's disease. It must be ruled out by obtaining negative Wasserman and Kahn tests. The history may also yield some information of value.

Chronic malaria must be ruled out if the patient has ever lived in or passed through a malarial district. A carefully taken history should serve to do this.

Idiopathic Purpura Haemorrhagica There is no history of hematemesis and the spleen is usually no larger than enough to be barely palpable. The number of platelets is as a rule lower and the white blood count is higher than in Banti's disease.

In Hanot's cirrhosis there is a greater prominence of hepatic symptoms. The markedly progressive enlargement of the liver and the attacks of fever with leucocytosis should establish the differential diagnosis.

Portal Cirrhosis.—Splenomegaly occurs in this disease. Enlargement of the spleen is usually most marked in the later stages when portal obstruction has become evident. The disease is then differentiated from Banti's by the history which points to the hepatic condition as being the primary one. In those cases in which the splenomegaly and cirrhosis appear to have arisen simultaneously the diagnosis may be difficult. As a general rule however if leukopenia and a low platelet count are present one is justified in diagnosing Banti's disease.

In Hemolytic Icterus there may or may not be a history of a similar condition being present in other members of the same family. There is a constant finding in this disease of increased fragility of the red blood cells, and this test should always be carried out to differentiate the two diseases.

In pernicious anaemia with its history of remissions the spleen is not so large as in Banti's disease. The high colour index, the presence of macrocytes in the blood smear, and the absence of free HCl in the stomach should serve to differentiate the condition.

Prognosis in Untreated Cases.

Spontaneous recovery is not known to occur. There may be minor remissions but as a rule the disease progresses steadily until the patient dies either from haemorrhage or from intercurrent infection. Most commonly, of course, bronchopneumonia. The prognosis after splenectomy will be discussed later.

Treatment.

Removal of the spleen when possible is at the present time the only logical treatment. Preliminary treatment prior to operation should aim at increasing the patient's general condition by means of rest in bed, nourishing diet and blood transfusion. Mackechnie advises a thorough course of X-raying before operation to decrease the size of the spleen and facilitate its removal.

Blood transfusions and continuous intravenous injections during the course of the operation have of late years been the means of saving the lives of many patients subjected to splenectomy. After operation the patient should be kept in bed for a reasonable length of time until the Hb has increased to 70 or 75 per cent. The administration of iron at this stage is possibly of benefit in decreasing the anaemia.

The effect of the operation on the blood picture is as follows:

The red blood cells are immediately increased in number. This increase in some cases amounts to a mild transient polycythaemia. The haemoglobin increases more slowly.

There is an immediate rise in white blood count often amounting to a mild leucocytosis. This rise is due for the most part to an increase in granulocytes. The relative lymphocytosis is then no longer present. After splenectomy the number of platelets in the blood stream is enormously increased.

Prognosis Following Splenectomy.

The prognosis after removal of the spleen is based upon the following factors:

1. The stage of the disease in which the operation is performed. Obviously in the first stage the patient is a far

better operative risk. In this stage also one can expect a more distinct and lasting improvement often amounting to a complete cure because the disease has not progressed to the stage of liver damage. Even in the third stage of the disease, however, splenectomy is probably of value. Krumbhaar reports on twenty cases operated on in this stage. Five of these succumbed to the operation, at least three were not materially helped and died within a few years as they would have done in any case, but twelve were manifestly improved.

2. The second factor in the prognosis after splenectomy is the platelet count before operation. Rosenthal's five cases with markedly diminished blood platelets all recovered good health without post operative complications following removal of the spleen. The four patients with normal or only slightly decreased platelets counts showed after operation a very marked increase in platelets, and all of them had signs of venous thrombosis. One of them died within a couple of days of the operation. In two the anaemia was only temporarily benefited. One apparently recovered. If Rosenthal's observations are correct, the lower the platelet count before operation, the better the prognosis after operation. The present mortality rate following splenectomy is between 10 and 20 per cent.

The Differential Diagnosis of Swellings in the Neck.

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It is obviously impracticable in a short article to discuss the diagnosis of each disease which may be a factor in the production of a swelling in the neck, and therefore the following remarks will be limited to the consideration of the nature of the enlargement and, from its various characteristics, what particular condition may be suspected as the cause. Only practical points in differentiation are mentioned.

A. General Enlargement of the Neck.

1. Apparent.

In short, stout individuals and those with unusually short necks an appearance of a general swelling is often given which is merely due to their build.

2. True.

Interference with the venous return from the head and neck produces a general enlargement and when the patient is well nourished the distension of the larger veins may, to a great extent, be masked. Oedema of the tissues is an added factor. Failure of the right ventricle, emphysema, and pressure effects of tumours in the superior mediastinum are the chief causes. Systolic swelling of the neck occurs in aortic insufficiency due to the high pulse-pressure.

B. Local Swelling.

Lymph Gland Enlargement.

This the most common abnormality in the neck. The recognition of lymph nodes, as such, is easy when the process causing the enlargement does not destroy their form and arrangement. The various groups are well known and the deeper ones are the more important. Enlargement of those beneath the sterno-cleido-mastoid may be distinctly palpable but tend to produce bulging of the muscle.

1. Inflammatory Swelling.

The more acute the process, the firmer, larger and more tender will the

gland be. When the adenitis is severe enough to involve the periglandular tissues, suppuration often follows. More chronically infected glands also involve the periglandular tissues, becoming adherent to neighbouring structures, to each other, and even to the skin. Since an inflammatory mass may arise anywhere in the neck either as an extension from deeper organs or as a localized cellulitis, it may be impossible at the time when first observed to decide whether or not the origin was lymphglandular. In general, cellulitis has ill-defined limits with a great tendency to a more widespread oedema of the surrounding skin and subcutaneous tissues than is usually seen in lymphadenitis. While no rigid rule holds as to the arrangement or grouping of enlarged glands in various conditions yet a certain tendency is frequently noticed.

Tuberculous adenitis: The deep cervical glands are those most affected at first. These appear as a mass at the angle of the jaw just in front of, or behind, the sterno - cleido - mastoid muscle. This chain of glands following the carotid artery is usually involved. The glands gradually become adherent to each other and to the deeper tissues until an irregular mass is produced in which individual nodes are indistinguishable. Areas of softening occur and fistulae may form. While the process is usually bilateral the advanced condition is most often only on one side.

Syphilis: In the secondary stage glands are frequently found to be enlarged in the posterior triangle of the neck. They are not much increased in size but are firm and "shotty."

Infectious mononucleosis (Glandular fever): This benign disease effecting children and young adults is marked by the symptoms of an acute infection with general glandular enlargement of moderate degree. The nodes may be painful as well as tender. The spleen is enlarged and the blood shows a moderate leucocytosis with 50 per cent. to 70 per cent. mononuclear cells. The acute symptoms last about two weeks but the glands may remain enlarged for months.

Hodgkin's Disease: Though not proven to be so, this disease behaves in many ways in the manner of an infection. The glands themselves usually do not suggest an inflammatory process. Those beneath and behind the sternocleido-mastoid muscle are most frequently affected. The pronounced enlargement is usually unilateral but the opposite side is involved and becomes more so as the disease progresses. The process spreads to adjacent groups of glands above the clavicle, in the axillae, and in the superior mediastinum. The glands are smooth and elastic. At first soft, they soon become firm. Even in large masses they remain discrete and not attached to neighbouring structures or to the skin. In long standing cases, and especially after repeated X-ray treatment, these characteristics may not hold true. They exhibit no inflammatory reaction but in the more acute cases tenderness may be present, depending perhaps on the rapidity of the swelling. Of the rest of the clinical picture one may mention: its exacerbating-remitting character; the periods of fever; the moderate enlargement of the spleen; the anaemia with some leucocytosis (occasionally leucopenia); the gradual general glandular involvement; and, in some cases, the severe generalized pruritus.

2. Non-inflammatory Swelling.

Carcinoma: Metastatic carcinomatous glands are typically almost stony hard, and the surface loses its smoothness. The nodes become adherent early. The condition is frequently bilateral but often much asymmetry exists—depending on the site of the primary.

The deep cervical chain is involved in carcinoma of the tongue and mucous membrane of the nasopharynx. It is noteworthy that the cervical glands

may reach a large size before a primary growth in the pharynx can be seen except by a minute search with the aid of a mirror. Carcinomatous glands at the root of the neck are most often secondary to breast, thyreoid, oesophageal and laryngeal carcinoma and, rarely, in carcinoma of the stomach a gland at the inner end of the left clavicle may be enlarged (the so-called sentinel gland).

Lympho-sarcoma: The neck is a common site for this condition. The glands form large masses and do not tend to remain discrete. Other groups of lymphoid tissue may show some enlargement but usually only after the main mass has become very large. The growth is fairly rapid, fever, if any, is slight, and the spleen is practically never involved. X-ray treatment often diminishes the size of the tumour for a time. There is no special finding in the blood counts.

Acute lymphatic leukaemia: Glandular enlargement in the neck may make its appearance later than most of the main symptoms of high fever and haemorrhage from the gums, nose and into the skin. If the disease is less acute the lymph gland swelling may be the first point noticed. The nodes remain soft and are discrete. The spleen is moderately enlarged and the blood picture, with the great lymphocyctosis and rapidly progressive secondary anaemia, makes a clear case. The patients are usually under twenty-five years of age.

Chronic lymphatic leukaemia: Occurring later in life than the acute form, the glandular enlargement is gradual and of a non-inflammatory character. Though earliest seen in the neck, the lymph nodes all over the body increase in size. The spleen is slightly enlarged and the blood shows a lymphocytic leucocytosis in most cases. On those puzzling occasions when an aleukaemic state exists, the differentiation from Hodgkin's disease may be most difficult. More rarely, there may even be a leucopenia. A relative lymphocytosis as a constant part of the clinical picture suggests leukaemia and examination of an excised gland may help to decide the point.

Myeloid leukaemia shows general glandular enlargement, the spleen is huge, and the blood picture is characteristic.

Thyreoid Gland Enlargement.

Swellings of the thyreoid gland are recognized by their position and by the fact that they move with the larynx on swallowing. They consist of four main types, namely: (a) A diffuse smooth surfaced hyperplasia which may be unilateral or involve both lobes and the isthmus. Physiological general enlargement is often seen at puberty. Pathologically it occurs as part of the clinical picture of Graves' disease. It is then softer (except after iodine administration) and a bruit may be heard over it. (b) An adenomatous type, where there are one or more nodular swellings of greater density and with a rougher surface than the surrounding gland tissue. The range in size may be very great. (c) Colloid type producing large, firm, cystic masses in any part of the gland. These three types may coexist in any combination and, in the latter two, there is no necessary correlation between the symptoms of thyreoid dysfunction and the type or degree of enlargement. (d) Carcinoma is an adenomatous type. The extreme hardness, the greater irregularity of the surface, the adherence to other structures, and the presence of metastatic lymph glands suggest the malignant nature.

Thyreoiditis: Inflammatory swelling may affect either part or whole of the gland and usually occurs as a complication of an infectious disease. Suppuration may supervene.

Vascular Swellings.

1. Venous: Bilateral enlargement has been mentioned. Unilateral enlargement may be due to local causes of pressure on the innominate veins, or

at a higher level from bony tumours of the clavicle and sternum or from a cervical rib. In myocardial failure the veins on the right side often show distension before those on the left. Phlebitis produces a firm venous tumour.

2. Arterial: The necessary feature of arterial swellings is a true expansile pulsation. An exception to this rule is when thrombosis has occurred in an aneurysmal sac. A mass lying closely adherent to an artery may give a first impression of a vascular lesion, but the transmitted pulsation is not expansile. A swelling in the episternal notch is produced by an aneurysm of the transverse part of the aortic arch. The pulsation is slow, heaving and forcible, and a systolic thrill and murmur, and a tracheal tugging may be present. Aneurysms may occur in the arteries of the neck in syphilis, in bacterial endocarditis, and as the result of trauma. Arteriovenous aneurysm occurs most often from trauma but may be congenital. A continuous humming-top murmur is heard over the tumour.

Swelling of the Salivary Glands.

The submaxillary and sublingual salivary glands may be involved in mumpc. In Mikulicz's disease the salivary and lachrymal glands are enlarged.

Enlargement of Nerves.

Neuromata may give rise to painless tumours. In von Recklinhausen's disease neurofibromata are to be found in the neck as in other situations.

Cellular Tissues.

Fatty tumours are not infrequent above the clavicle, forming variably sized masses as encapsulated nodules or circumscribed swellings, often painful. They may be multiple and symmetrically placed. In the condition 'adiposa dolorosa' symmetrical deposits of fat occur in various parts of the body and frequently in the neck. There is spontaneous pain as well as pain on pressure.

The cellular tissues and muscles are frequently the site of inflammatory lesions as in furunculosis of the skin, erysipelas, pyaemia, and mycotic infections. Sebaceous cysts may give rise to large superficial swellings.

Finally, one must decide when the tumour is in the upper part of the neck whether it is arising from the lower jaw.

When its nature, and the probability of the origin of a swelling in the neck is determined then a correct diagnosis will be made, most frequently in an order something like this:—

Common conditions

Infected lymph glands—various infectious fevers; various local nose and throat infections.
Tuberculous adenitis.
Erysipelas.
Distension of veins in emphysema and heart failure.
Colloid goitre; adenoma of thyreoid; hyperplasisa of thyreoid.
Furunculosis.

Less common conditions

Infectious mononucleosis.
Myeloid leukaemia.
Thyreoid carcinoma.
Metastic carcinomatous glands from nose, throat and tongue.
Sebaceous cysts.
Enlarged thymus.

Rare conditions

Gummata.
Acute lymphatic leukaemia.
Dengue.
Sarcoma of jaw.
Actinomycosis of jaw.
Lymphosarcoma.

Very rare conditions

Aneurysm.
Neurofibromata.
Fungus diseases.
Diverticula of osesophagus.
Thyroglossal cyst.
Arteriovenous aneurysm.
Mikulicz's disease.
Branchial cyst.
Parathyroid tumour.

The Etiology and Treatment of the Common Cold.

By M. J. KELLY, 3T0.

It seems strange, in this very advanced period of scientific knowledge and research, that the etiology and treatment of this extremely prevalent condition, common colds, should go undiscovered. It is significant that numerous workers are turning their attention to a broader field than that of a study of the respiratory tract alone and are looking for a more generalized body disturbance, to certain changes in metabolism and to variations in environment, climate and diet. The very conflicting evidence in the strictly infectious theory of colds leads one to believe that the fundamental causes will yield themselves to just this type of further research.

A common cold is usually described as an acute infection of the upper respiratory tract. However, many authorities state that it has not been satisfactorily shown that any of the numerous organisms found in the nose, throat and mouth are the cause of colds. The clinical aspects have been sadly neglected, as a cold is usually looked upon as a trivial affair which must run its course, treatment not being of much avail. That the common cold is a trivial affair is entirely erroneous. In industry time lost on account of colds is a serious economic problem. Statistics have been brought forward to show that sickness causes a loss in industry of ten calendar days per year per person, and of these persons five out of every ten are absent with colds. The result of this is naturally decreased efficiency, decreased production, lost time and extra expenditure.

There has been a dearth of research work on the etiology except for considerable theorizing, which seems for the most part to remain theory. From a bacteriological point of view the etiology revolves around a primary infection by certain single organisms, groups of organisms or by a filtrible virus. Therefore it is generally accepted that this strictly infectious theory of the cause of colds has not been proven. Evidence which in part seems to contradict this theory is that secretions from the nose in the early stages of the disease are for the most part found to be sterile. Later in the disease the bacteria which are usually regarded as the causative organisms appear in the secretions, but it is probable that they are really only secondary inhabitants.

Extensive work by an investigator, V. S Chesney, showed that innoculations with nasal secretions of patients suffering from colds have failed to produce a similar infection and similar symptoms. This leads the investigator to believe that the epidemics of colds in families, factory workers and similar groups are due rather to a similarity of living conditions and common unhygienic surroundings resulting in altered metabolism bringing on systemic changes which affect the various secretions and fluids of the body.

With regard to the views on the effect of climatic conditions such as cold, dampness, wind and sudden changes in temperature, it is agreed that all are excitory and contributory factors and that they have a marked effect on the heat-regulating centre. However, despite their very important role in the production of colds we know that the heat-regulating centre in health is not easily disturbed and that the above factors are contributory rather than causative. A notable contribution on this subject is some statistics by Barron, which indicate that the incidence of colds at Stanford University in an exceptionally agreeable climate is about the same as among comparable groups of students at Cornell and Harvard in a region of extremes of climatic conditions. Also in this regard a study has shown that

whether students at these institutions used sleeping porches, well ventilated bedrooms or poorly ventilated bedrooms, does not appear to affect materially the susceptibility to catarrhal colds. Of course, the morbidity is slightly higher in those using poorly ventilated rooms, but the difference is not sufficient to warrant any definite conclusions. Thus climatic variations are contributory only in as much as they inhibit normal activities and decrease such factors as protein utilization. It is a well-known fact that people eat too much and exercise too little in the winter months when colds are prevalent. To substantiate this it is known that colds are much more prevalent in those engaged in indoor work than in outdoor work, such as lumbering, where muscular exercise is carried on even in extremes of temperature, and colds are practically absent.

Chesney, in his study of a large group of cases, found very definite changes in the body chemistry of patients whom he treated for common colds. A more acid urine was noticeable in all cases. He found that the CO_2 combining power of the blood sugar was also low as well as the non-protein nitrogen. The Basal Metabolic Rate was on the negative side in most instances. From these very definite findings it is seen that the blood chemistry is decidedly altered and as a consequence the tissues of the body are supplied by an abnormal fluid. There is a noticeable decrease in the reserve bases and the bicarbonates in the plasma and a condition of acidosis exists. All of these findings lead one to conclude that common colds are merely a local manifestation of a systemic disturbance mainly in the acid base equilibrium and in the protein and carbohydrate metabolism. The symptoms of colds of different degrees have been induced by artificial acidosis and have been relieved by changing the blood back to its proper reaction.

The symptoms of cold vary with the severity of the attack, and may range from a coryza with mild pharyngeal and nasal irritation to cases with severe headaches, muscle pains, lassitude, anorexia and malaise. These may have their sequelae in laryngitis, pharyngitis, bronchitis, la grippe, influenza, pneumonia, ottis media, sinusitis and a host of other complications, so that it is essential that early colds be abated and that well-developed ones should be very vigorously treated.

In consideration of the treatment it is well to deal first with the contributory factors which play an extremely important part. One should in the first place arrange a diet which will be in proportion to the amount of exercise, in this way preventing overeating. The use of more carbohydrates and fats to produce the proper amount of heat is essential. Exposure to extremes of cold or dampness should be carefully guarded against, but there should be a definite effort to condition the body to such extremes. The proper humidity, temperature and air movement in residences and places of business should receive strict attention. The body should not be dressed too warmly, as it will become over-sensitive to changes in temperature and external conditions. Overwork, either physical or mental, leading to fatigue, has a tendency to lower vitality and constitutes a predisposing cause that is to be guarded against as much as possible.

Regarding specific treatment—rest, hot drinks, sedatives for a useless cough and expectorants to assist the so-called second stage of a cold, are very helpful. Based on the finding of altered metabolism found in colds, the investigators have a particular plan of attack.

In the early stages when the main symptoms are dryness of the pharynx, with slight coryza and congestion of the mucous membranes, alkalinization is induced by large doses of sodium bicarbonate until the urine is alkaline to litmus. Doses of 60 grains of sodium bicarbonate followed by a large glass of hot water every two hours, for three doses, with the addition of one grain of

calcidin every half-hour for 6 doses, will in most cases shorten a cold.

For colds which have advanced further the treatment is a little more vigorous. An initial dose of 60 grains of sodium bicarbonate with 1 grain of calcidin is followed by 30 grains of sodium bicarbonate and 1 grain of calcidin every 2 hours for 6 doses, then 20 grains of sodium bicarbonate with 1/3 of a grain of calcidin every 3 hours of waking until the cold is cured. Coincidentally prophylaxis is maintained by exercise and a diet which is well balanced and thoroughly adapted to the individual's physical activities.

It is an error that common colds cannot be successfully and quickly treated. The various factors contributing to the body upset must receive strict attention and with constant physical fitness and early, vigorous treatment on the slightest symptoms, a great deal of inconvenience suffered by individuals, and the severe economic problem the situation presents could be avoided.

The Formation of the Aqueous Humour.

By G. B. WHITE, B.A., M.D. (London, Eng.)

It has long been conceded that the aqueous humour of the eye is formed by the ciliary body, but the exact mode of formation has ever been a subject for argument. The old theories were that it was either a secretion or a transudate from the blood.

The secretion theory was based purely upon the anatomical structure of the ciliary processes, with their tufts of capillaries resembling the glomeruli of the kidney. But there is no physiological nor pathological basis for this assumption. By a secretion is meant the elaboration of one substance from another, and if the aqueous were a secretion, we would expect its constituents to differ from those of blood plasma, whereas they are qualitatively identical. Moreover, secretion involves the liberation of energy, and there is no energy expended in the formation of aqueous.

If the aqueous were a transudate, its constituents should be not only qualitatively, but also quantitatively, identical with the blood plasma, and this, as we shall see, is not the case.

In recent years a new theory has been propounded, that the aqueous is a dialysate of the blood. By dialysis is meant that process in which when a complex solution, containing colloids and crystalloids, is brought into contact with a semi-permeable membrane, some of the water passes through the membrane, taking with it some of the diffusible crystalloids, but not the non-diffusible, large moleculed colloids. The process ceases when the fluid on both sides of the membrane (known parent solution and dialysate) are in equilibrium. A true dialysate will thus contain no colloids. Of the crystalloids, some are ionised and other non-ionised. The latter will be present in equal concentrations on both sides of membrane, but of the ionized, the parent solution will retain a comparative excess of positively charged ions, while the dialysate will be richer in negatively charged ions. Further, the multiple of the quantities of positive and negative ions on one side of the membrane will be equal to the multiple of the similar quantities on the other side.

The constituents of capillary blood cannot be measured quantitatively, but those of arterial and venous blood can be, and the quantities in capillary blood may be assumed to be intermediate between the quantities in the arterial and venous blood.

Now it is found that the quantity of non-ionised crystalloids in the

aqueous is intermediate between the quantities in arterial and venous plasma and may therefore be assumed to be equal to the quantity in the capillary stream. Of the ionised diffusible substances, positively charged ions are greater in the plasma than in the aqueous, while the negatively charged are less; and the multiple of the amounts of positive and negative ions in the plasma is equal to the multiple of these amounts in the aqueous.

Eg., Na x Cl = Na x Cl.
(Blood) (Aqueous)

Thus, as far as the diffusible substances are concerned, the aqueous is identical with a dialysate of the blood plasma. But if it were a true dialysate, it should contain no colloids, whereas colloids are present. But their amounts are very minute, considerably less than the colloid constituents of plasma, and therefore considerably less than would be expected in a transudate from the plasma, but no more than could be accounted for were the capillary walls not entirely impermeable to the large colloid molecule.

If the aqueous were a transudate, it might undergo any number of quantitative or qualitative changes, whereas a dialysate can only undergo changes from two causes, either changes in the permeability of the membrane, or changes in the composition of the parent solution. It is found that all changes in the aqueous are of one of these two types. Thus if the capillaries are dilated, their permeability is increased and the aqueous becomes richer in its colloid contents, while with changes in the composition of the blood, the colloids of the aqueous remain constant, while the crystalloids maintain an equilibrium with the blood crystalloids on a new level.

Hence, the preponderance of recent evidence appears to point to the aqueous being a dialysate of the blood plasma, rather than a transudate or secretion.

Hare-Lip and Cleft Palate.

By K. R. BAXTER, 2T9.

Hare-lip and cleft palate are two conditions all too frequently encountered in the new-born child. They may be present singly or be present in association with each other, and are due to maldevelopement in intra-uterine life. If untreated, the child is liable to die in the early months of life due to its inability to obtain sufficient nourishment, or to more general causes such as diarrhea, pulmonary trouble and exhaustion. If it survives to early childhood it will be permanently disfigured, and, at a great disadvantage in eating, in appearance, and in speaking. However, if treated in the proper manner and at the proper time, no permanent disability results and the amount of facial disfigurement is negligible.

While these two conditions are very closely associated, we shall discuss each separately, and then in summarizing draw more general conclusions.

Hare-lip may be defined as a congenital fissure of the upper lip which may extend for a variable distance through the soft tissues alone, or may also involve the bony alveolous and the floor of the nose, and extend backwards through the palate. In reality the name is a misnomer, since a hare's-lip is cleft in a Y-shaped manner the fissure being central below and bifurcating above into each nostril.

Embryological Development. — In studying the causative factor of hare-lip one studies the development of the head between the 5th and 10th weeks of intrauterine life. The bony and fleshy parts of the face originate from

the outgrowth of processes around the cavity formed by the bending forward of the primitive cerebral vesicle over the end of the notochord. The integrity of the upper lip is obtained by the union of the lower parts of the internal nasal and mixillary processes, which thus exclude the external nasal from participation in its free border. At the same time the deeper parts of these processes are uniting with one another and with the palatal plates which grow horizontally inwards from the under side of the maxillary processes, uniting in a Y-shaped suture, the point of junction of the limbs being situated at the anterior palatine canal. The union of all these elements is taking place from the 6th to the 10th week, and by that date even the uvula, the last part to unite, should be complete. Ordinary hare-lip then, is due to a failure of union of the internal nasal process with the structures in external relation with it. If limited to the soft parts, the cleft runs between the Internal nasal and maxillary processes. If complete or alveolar, it runs between the same two below and superficially, but in addition the cleft is between the internal and external nasal processes above. The cleft in the alveolus passes between the maxilla and intermaxilla.

Varieties. — Hare-lip may be single or double, i.e., unilateral or bilateral. It may be complete or incomplete according to the degree of its extension. It is termed simple if limited to the soft parts; alveolar if the bony alveolus is also involved, and complicated if associated with a cleft palate. If the hare-lip is unilateral it is most common on the left side, in the proportion of two to one. If bilateral it is usually, but not invariably, alveolar and accompanied by a complete cleft of the palate. The central portions of the lip and alveolus may retain either their normal position, or as is more frequently the case in the bilateral type, project forwards at the end of the nose. Even in simple cases the nose is deformed, being broad and flattened. Hare-lip is not uncommonly associated with other deformities, such as Spina-Bifida, and is frequently transmitted from one generation to another.

Age at Operation. A great divergence of opinion exists as to the best time for operation. The rule of British surgery is to get the operation over before dentition begins, whereas the German surgeons defer taking any steps until the child has entered upon his second year. Others again say the operation should be performed as soon as possible after the first day of life, providing the child is healthy. However, taking all things into consideration, providing the child is healthy and in good condition, any time between the 3rd and 6th months is preferable. It is better to allow the infant an opportunity to get over the shock of its entrance into the world, and become acclimatized to an independent existence, whilst at the same time, the operation should be performed before the troubles of dentition begin. Another argument for deferring operation until between 3rd to 6th month is that it can be done much more perfectly and artistically on a young child than on a new-born infant, the parts being larger, more fleshy, and more easily handled. Sutures also cut out less readily.

Another question in dispute is that if the hare-lip is complicated by a cleft palate should both operations be performed at the same time and if not which should precede? It used to be generally agreed that where this condition exists, the cleft palate should be operated upon first, as the smaller mouth resulting from the operation for hare-lip greatly diminishes the accessibility to the palate. However, the reverse is true now, the hare-lip being operated on about the 6th week and the cleft palate at about 18 months. Here in Toronto, the practice is to repair the hare-lip about the 6th week of life providing the child is healthy and where cleft palate coexists, to repair it at about 1½ years of age.

This latter age is chosen because the child has not formed a very large vocabulary, and the permanent teeth have not started to grow. Moreover the operation should be performed in the summer time to guard against respiratory complications and other sequelae. If the hare-lip is uncomplicated then any time from 6 to 12 weeks is a good age at which to operate — in well-nourished and healthy children at the earlier date, in poorly-fed and weakly children at the later, unless the inanition is due to the difficulty in feeding the infant owing to the deformity, when the operation will have to be performed during the first weeks of life.

Operation. Many and varied indeed are the methods of repair of a hare-lip. They vary in technique depending on the cleft being single or double or complicated, etc. In all these the underlying principle is the same. The child is laid on the operating table with its arms and legs bound down. The surgeon stands behind, with the anaesthetist and assistant, one on either side. The first step in the operation consists in thoroughly dissecting up the lip from the maxillae and alveoli, by cutting through the reflections of mucous membrane and the attachment of the muscles and other soft parts. To render the separation efficient, the knife must sometimes be carried up to the infra-orbital foramina, while the alae nasae must also be thoroughly separated so that any flattening and distortion of the nostril may be remedied. The edges of the cleft are then pared, the object to be attained being the union of the cleft lip by means of a cicatrix, which shall be as unobtrusive as possible whilst the red margin must be continuous and the section such that the raw surfaces are larger than are absolutely necessary so as to allow for subsequent cicatricial contraction without the development of a notch.

The first stitch is inserted at the apex of the cleft or within the nostril, and the second is inserted at the red margin to insure of correct apposition. Allowance should be made for the contracture of the scar tissue which will invariably take place. If the operation ends with a symmetrical looking mouth, the result will not be good, because a dimple will occur in 4 to 5 years as a result of scar contraction. At the close of the operation there should be a slight redundancy or fulness of tissue at the edge of the lip in the line of the cleft. The wound is dressed with a small piece of gauze and secured by another dry piece cut in the shape of a butterfly. This is fixed by collodion. The child's hands should be restrained by means of splints over the flexor surface of each elbow.

Repetition of Operation. In some cases this operation for repair of hare-lip may have to be repeated several times. Where primary union fails, all sutures should be removed, and the parts fomented with boracic acid. As soon as all inflammation has subsided the edges will rapidly become covered with healthy granulations. An anaesthetic should now be given and the parts thoroughly cleansed and dried. They are then carefully approximated with gauze and collodion over which a strapping should be applied to maintain position.

Post-Operative Treatment of these cases is very essential. They should be fed very carefully and kept very quiet until such time as the incision heals. When the child begins to talk, proper voice culture should be taught.

Causes of Failure and Death after Hare-lip Operations. 1. The chief cause is the lack of vitality and resistance of the child prior to operation. Some of these children suffer from Marasmus, and whether operated on or not, will die in infancy. 2. Haemorrhage is a factor and is due to very free separation of the flaps in a weakly child or to the arteries not having been properly secured. Loss of blood may lead to non-union, and it may also destroy life rap-

idly by a clot in the fauces and upper aperture of the Larynx. 3. Bronchitis and broncho-pneumonia. To guard against these, the operation should never be performed during the cold and damp months. 4. Diarrhoea. 5. Asphyxia. 6. Infection.

Cleft Palate may be defined as a congenital defect of the roof of the mouth whereby the structures entering into its formation do not unite in the mid line, thus allowing an abnormal communication to exist between the nose and the mouth. The mildest cases consist merely of a bifid Uvula, perhaps not involving the palate at all. The next degree affects the Velum alone, more or less of the hard palate may also be implicated, the cleft reaching as far forwards as the site of the Anterior Palatine canal. The severest type of deformity extends through the alveolus and upper lip on one or both sides. The union of the palatal segments takes place from before backwards, so that it is very unusual to find the alveolar portion of the palate affected apart from the rest.

Embryology. To gain a true conception of this condition requires an understanding of its causation. In early foetal life, the nose and mouth make one cavity. At the eighth week the palate begins to grow in from either side in the form of two horizontal processes. These processes meet and coalesce in the mid line, but when their development is arrested, a median cleft of the palate results. This may be complete, or the processes may unite in some of its parts in front or behind. The roof of the mouth is not wholly formed by these two processes, one will recall. In the mid line and anterior to them a median process of mesoblastic tissue comes down from above and goes to make up the front part of the hard palate, the anterior part of the nasal septum and the middle portion of the upper lip. The intermaxillary bone is represented in this tissue. When this intermaxillary process fails to unite with the rest of the maxilla, a lateral cleft results. Such a cleft may be on one or both sides and is found running through the base of the nostril. Thus the cleft in cleft palate which is required to be repaired may be represented by a Y or any of its parts. The anterior intermaxillary process may be dislocated forward if both arms of the Y fail to unite, so that a median portion of the lip and palate, together with the alveolar process may project forward. For this reason cleft palate is apt to be associated with hare-lip.

Varieties. The extent of the cleft may vary immensely. Every intermediate stage may be found between a bifid uvula and a complete cleft of both the hard and soft palate associated with a single or double hare-lip. A cleft of the hard palate without any cleft of the soft palate is rare. The cleft may be narrow, or so wide that the palatal processes appear to have developed but slightly. The nasal septum may end freely below or be attached to the palate at one side of this cleft. The results of the deformity are the well-known nasal indistinct speech, difficulty in swallowing, and regurgitation of food thru the nose. With a complete cleft of the palate and lip, an infant is unable to take the breast, a difficulty which, however, can usually be overcome by constant care and attention. With regard to the voice, even when the cleft is neatly closed, this operation is often very disappointing as regards speech. This is due to the fact that the repaired soft palate has lost much of its mobility and hence cannot shut off the naso-pharynx from the buccal cavity.

Optimum Age for operation is anywhere from 1½ to 2 years of age. It is found that if the operation is postponed until this age, the cleft has narrowed considerably. Especially is this true where the alveolar process is involved, and where a coexisting hare-lip has been operated upon in infancy. The perfect palate operation should

enable the patient to speak well, to eat well, and by the reproduction of the normal facial contour to look well. The diagnosis rests on an estimation of the loss of tissue, the displacement of tissue and the consequent loss of function. This brings up another question. Is cleft palate due to a loss of tissue, or to a displacement of tissue due to the fully developed parts failing to unite. There are advocates of each theory and consequently different forms of operation to suit each theory. By loss of tissue is meant that tissue is lacking owing to mal or non-development. By displacement of tissue is meant that no loss of tissue exists, but merely that the fully developed parts have failed to unite. By loss of function is meant disturbances in relation to mastication and articulation. Thus it may be seen that the results to be desired following a cleft palate operation are:—

1. Freely movable soft palate so that the naso-pharynx may be cut off at will.

2. Mastication must be good, with no regurgitation of food through the nose.

3. That the patient be able to speak all words, syllables and sounds fluently.

4. That the natural contour of the face be restored.

Preoperative Treatment is very essential. First of all the child should be in the very best of health. It should be in the hospital for several days prior to operation, so that it may become accustomed to its nurse and surroundings. If tonsils or adenoids are enlarged, they should be removed several weeks previously. In short all avenues of infection should be excluded.

Operation. Three main types of operation have been advocated and these more or less depend upon whether the surgeon believes in the loss of tissue or the displacement of tissue theories. Names associated with these various forms of operation are:

1. Langenbeck, Smith, Berry.
2. Davies, Colley, Laire.
3. Brophy.

Langenbeck's Operation for repair of a cleft involving both the hard and soft palate, is the one most frequently performed and gives excellent results. Very briefly it consists of the incision and detachment of the Muco-periosteum. The knife is inserted close to the last molar tooth and about half an inch from the aveolar margin and carried forward parallel to the teeth to a spot just anterior to the apex of the cleft. The muco-periosteum is divided down to the bone, and the soft structures of the palate are stripped up toward the middle line until the point of the instrument is seen protruding into the cleft. This procedure is carried out on both sides. The edges of the cleft are then pared. The anterior portion of the cleft is then drawn together with silver wire while the uvula is sutured with silk.

Laire's Method of Treatment is more applicable to young children within a few weeks of life. Briefly it consists in raising suitably shaped flakes of muco-periosteum from either side of the palate, in such a manner that when turned over they can be sutured one to the other and thus form a complete barrier between the mouth and the nose.

Brophy's Operation follows out the theory that Cleft Palate is due to the displacement of normally developed tissue. It aims at closing the palate by drawing together the bony maxillae. The margins of the cleft are pared and stout silver sutures are carried through the maxilla from side to side just above the palate. The ends of the silver wire are passed through holes in lead plates and drawn tightly together by twisting. The maxillae are forced together by digital pressure so as to approximate the margins of the palate and the wires, are then tightened as deemed necessary.

Many, indeed, are the variations of the three preceding types, but essentially they are as given.

Post-Operative Treatment of these cases is very important. The child should be put to bed with the head low so as to facilitate the drainage of accumulated blood. No food should be given until the risk of vomiting has passed. For the first forty-eight hours only sterile water and milk should be given, later increasing to a Sippy diet. The wound should be left alone, the child's hands restrained, and the nurse should devote her time to preventing the child from crying and keeping it amused. Infection, too great tension, or too little blood supply may cause failure of union. After the wound has healed by far the most important after-treatment begins—namely the improvement of speech. As a result of the operation speech will be impaired, since the mechanism which the patient ordinarily employs is thrown out of gear, and consequently education by a voice-trainer is absolutely essential. Even then the unpleasant articulation persists occasionally owing to the patient being unable to draw up the velum so as to close the posterior nares. This is due to a reduction of the depth of the soft palate owing to the traction required to close the cleft. In spite of this, the operation is most beneficial in that it shuts off the nose from the mouth, prevents the dropping of mucous, improves the sense of taste and adds greatly to the general comfort of the patient.

Finally and in conclusion, while hare-lip and Cleft Palate, are in themselves serious complications they are easily amenable to treatment and in the hands of good surgeons, excellent results may be looked for.

The Treatment of Structural Scoliosis.

By E. C. JANES, M.B. (Toronto),
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With so little time at our disposal one cannot hope to touch upon the many aspects of so complex a problem as Scoliosis. I will, therefore, confine my remarks entirely to the treatment of the structural type, and present a patient, to demonstrate the most recent form of treatment for this condition.

All cases of Scoliosis may be classified as either Functional or Structural. This division is based on the pathology found in the spine. In the former, no bone change is found, and in the latter, there is bone deformity of varying degrees. These types may be subdivided according to etiology — iodiopathic, paralytic, congenital, rachitic, and secondary to other deformities such as torticollis, chest disease, short leg, etc.

This patient is 19 years of age. The etiology is Infantile Paralysis at 2 years of age. Frequently, the cause is obscure, but in this patient, the history is clear and there are other evidences of the disease.

He showed the cardinal signs of a severe Scoliosis — elevated shoulder, prominent hip, costal margin overlapping iliac crest, deviating spinous processes and prominent ribs on one side, due to rotation of the vertebrae. This prominence is more easily seen with the patient stooping. In Structural Scoliosis, it is always on the convex side of the curve, and in Functional Scoliosis, it is always on the concave side. This observation, and the fact that the deformity of functional cases disappears in recumbency, constitutes the method of differentiating the Functional from the Structural type.

The principle used in attempting to correct this patient's deformity, was that a curved rod will straighten if one pulls on both ends and exerts pressure on the convexity. By means of Buck's extension on each leg, and a halter on the head, extension up to 40 pounds was used. Plaster beds of graded heights were used, to exert pressure on the prominence. This treatment was continued for two months. The height increased 5 inches, and the line of the spinous processes became practically straight.

The spine was then fused by Hibb's method, from the third Thoracic to the fifth Lumbar vertebrae inclusive. In this operation, the spinous processes, lamina and lateral articular facets are exposed sub-periostially. The articular cartilage is destroyed, and multiple fragments of bone are cut from the lamina and spinous processes, overlapping from one vertebrae to the next. The periosteum is closed over these fragments, and when healing, is complete, the spine is fused by a continuous mass of bone, which prevents any movement between the vertebrae. The operation in this type of case, is technically very difficult, because of the extreme distortion of the vertebrae. It was necessary to do it in two stages. Each produced sufficient shock to require blood transfusion.

The patient is now walking, and wearing a plaster jacket to support the spine until the fusion becomes more solid, and sufficient new bone is produced to maintain the corrected posture.

Other operative procedures, all modifications of Hibb's fusion, have been devised. The most noteworthy is that of Whitman, who adds a heavy bone graft on the concave side of the curve. This graft is obtained either from the Tibia or the prominent ribs. It acts as a prop, and probably stimulates more rapid and greater bone production.

One may ask if such severe corrective procedures are justifiable, when the result cannot be absolutely guaranteed. I believe the answer is quite emphatically yes. Along with the spinal deformity, there is very marked distortion of the viscera, particularly above the diaphragm, with consequent embarrassment of circulation and respiration. Without correction, such patients rarely live to middle age. They live secluded, because of their deformity, and die early, usually from intercurrent infections. Ambulatory contrivances, such as celluloid and plaster jackets, are inefficent, and are too cumbersome and uncomfortable, to be worn permanently, so any method that offers reasonable success, should be welcome.

This boy has had five inches added to his height, he is no longer a hunchback and his general condition is already much improved.

The real treatment of Scoliosis is the prevention of the structural type. This depends on early recognition, and treatment while still in the functional stage, and therefore, puts one more burden on the family physician, who can diagnose the condition early, in many cases before the parents, themselves, have noticed anything wrong.

He should use suitable corrective exercises, and supports where necessary, or refer the patient to those who have the training and facilities for handling the condition.

Purpura and Haemophilia.

Etiology and Clinical Classification.*

By G. L. DUFF, M.A., 2T9.

Strictly speaking, purpura is a symptom, not a disease. However, under this term are conveniently arranged a number of diseases characterized by haemorrhages into the skin and mucous membranes. Before proceeding to a discussion of the etiology of such conditions, it may be profitable to consider some features of capillary structures and physiology, the normal structure and formation of blood platelets and the normal process of blood coagulation.

Capillary Structure and Physiology:

The walls of the capillaries consist of lining endothelial cells, the entire vessel being, in fact, a delicate endothelial tube. The endothelial cells composing the capillaries are elongated and possess oval nuclei. They are united by narrow lines of cement substance. In the smallest capillaries, two endothelial cells may suffice to encircle the entire lumen: in the larger three or four cells may be required to complete the vessel. The capillaries are usually arranged in networks, the component channels of which are of fairly constant diameter within a particular tissue. Their usual diameter varies between eight and twenty micra. Although preformed openings or stomata in the walls of the capillaries do not exist, the escape of leucocytes and, under certain conditions, also of red blood cells takes place between the endothelial cells. In some capillaries as in those of the choroid, liver or renal glomeruli, the usual demarcation of the wall into distinct cells is wanting, the individual endothelial cells being replaced by a continuous nucleated sheet or syncitium.

It has been shown by Vimtrup that the contractile structures associated with alteration of the lumen of the capillaries, are branched cells placed outside the endothelial walls of the capillaries. These cells were originally described by Rouget in 1873 and are called Rouget cells. They are a special variety of plain muscle cell placed at intervals along the capillaries and not forming a continuous layer. These cells are nucleated and possess long branching processes, which run around the circumference of the capillary and by their contraction narrow the lumen of the vessel. Their size, shape, structure and abundance vary in different organs.

The innervation of the capillaries is from non-medullated fibres, believed to be of sympathetic origin, which form a terminal nerve network of primitive type around the smaller vessels both capillaries and arterioles. On stimulation of the sympathetic supply, contraction of the capillaries as well as of the arterioles has been observed by Hooker and others. It seems equally certain that the capillaries have a vasodilator supply closely resembling that of the arterioles and leaving the spinal cord in the posterior roots (Bayliss).

The pressure in capillaries is low but variable. It has been measured in man by Carrier and Rehberg. It was found that capillary pressure in the hand, varies with the position of the hand with reference to the heart and may be as great as 30 cm. of water or as little as 4 to 5 cm. However high the hand was placed, it never fell below about 4 cm. of water. In the feet the capillary pressure is normally pre-

*The conclusion of this subject, "The Diagnosis and Treatment of Purpura and Haemophilia," by A. Appel, will appear next month.

vented from attaining very high values owing to the presence of valves in even the smallest veins and to the occurrence of small muscular movements which by forcing the blood into these veins permits them to act as a kind of pump.

The walls of the capillaries are readily permeable to water and crystalloids but the proteins and other colloids of the blood are normally held back more or less completely. It is quite reasonable to suppose that if the permeability of the capillaries were to be increased some of the smaller sized protein particles might pass through their walls and this seems certainly to be so. The most important fact in connection with capillary permeability is that it is increased under any circumstances which lead to dilatation of the capillary vessels.

There is no evidence that normal capillaries ever become permeable to definite particles. Krogh found that particles of India ink which were 200 millimicra in diameter and beyond the limits of visibility were unable to pass through the walls of even widely dilated capillaries. Soluble starch, however, which had particles of 5 millimicra in diameter, was kept back by contracted capillaries but passed through them when dilatation was produced.

Normal Structure and Formation of Blood Platelets.

The blood corpuscles are of three kinds: red corpuscles, white corpuscles and platelets or as they have been called by Osler, third corpuscles. For the purpose of this paper it will be sufficient to discuss only the platelets.

The platelets appear in fresh blood as hyaline, refringent, rounded but irregularly outlined, slightly granular bodies. They are smaller than red blood corpuscles and of varying diameter. Their number in normal blood varies with the method of counting but it is usually said to be 250,000 to 350,000 per cubic millimetre. Stained by the usual methods the platelets are blue with a variable number of small purplish granules. Vital staining of fresh blood with brilliant cresyl blue shows the platelets to contain a round or oval, faintly granular, purplish staining body, constituting about one-third of the volume.

In freshly drawn blood adjoining platelets immediately adhere to one another and form close aggregations of varying size, so that in smear preparations the platelets often occur in groups. It has been shown in certain animals that this tendency to stick together and to aggregate in groups is not manifested by the platelets while they are within normal blood vessels. It is presumed that the platelets in human blood behave in the same way. Under certain pathological conditions the platelets do adhere to one another within the vessels. Thus aggregations of adherent platelets form the essential element in recent thrombi while the clotted blood in them is secondary.

The red blood corpuscles, the granular leucocytes and the platelets are formed under normal conditions from cells of the red marrow of the bones. They are not capable of reproducing themselves. In early childhood the long bones as well as the flat bones contain red marrow while in the normal adult the red marrow is largely restricted to the flat bones.

Normal red marrow is composed of a parenchyma of marrow tissue proper, traversed at close intervals by a system of numerous blood vessels. The parenchyma consists of special kinds of cells and fat cells supported by a delicate stroma. The special cells infiltrate among the fat cells and are closely packed together.

The origin of the platelets is not conclusively proven but Wright believes them to be detached portions of one of the special kinds of cells of the marrow, the giant cell or megakaryocyte. These cells are larger than any of the other special cells of the parenchyma and are less numerous. They have a large lobed nucleus and

the cytoplasm contains numerous small granules identical in appearance and reaction with the granules in platelets. The megakaryocytes become larger and attain more granules until a maximum size is reached, when the cytoplasm is prolonged into pseudopodia by amoeboid activity, the granules aggregate in small groups and the cytoplasm breaks up into fragments, each containing a group of granules and constituting a platelet.

The life of platelets in the circulation is estimated at from 3 to 5 days.

The Normal Process of Blood Coagulation.

Blood clotting is dependent on the colloidal nature of the blood and the process seems to be essentially one of colloidal aggregation under the influence of calcium electrolytes. Surface tension is also a very important factor in coagulation. It is generally agreed by the more prominent investigators, except Nolf, that the final step in coagulation consists of a reaction between two substances thrombin and fibrinogen.

Fibrinogen is a globulin and occurs as such in circuating blood. It appears to be formed chiefly in the liver (Meek, Whipple) and thus it may be anticipated that with severe liver damage a haemorrhagic condition may ensue due to the diminution of fibrinogen.

Thrombin is a protein or protein derivative giving the tryptophane reaction. It does not occure as such in the blood. Its manner of formation is explained differently in different theories of coagulation. For the formation of thrombin, calcium salts must be present in a certain physical state. In addition to calcium, two other factors are required for the formation of thrombin. The first of these occurs in the blood stream as does the fibrinogen and calcium and is known as thrombogen or prothrombin. The main source of this substance seems to be bone marrow (Drinker and Drinker). The blood platelets are also an important source. The other factor necessary for the production of thrombin is thrombokinase, thromboplastin or cephalin. It is found in tissue juices and blood platelets and its nature is that of a lipoid.

In brief, then, clotting takes place by the formation of thrombin from prothrombin in the presence of calcium ions and cephalin or thromboplastin. The reaction between thrombin and fibrinogen causes the formation of fibrin and coagulation results.

Howell believes that prothrombin is kept inactive and protected from the activating influence of calcium ions by an inhibitory agent, referred to as antithrombin, so that the normal fluidity of the blood is maintained. He believes that cephalin exerts its accelerating action on coagulation by neutralizing the influence of antithrombin. Others believe its action to be that of an enzyme.

From the work of various investigators, it appears that there are other antisubstances besides antithrombin and these appear to be formed particularly in the liver. Their exact nature is unknown. One such antisubstance is a phosphatid existing in various tissues but found in great abundance in the liver. It is aptly called heparin. A second such substance is found in the plasma and serum. It is converted to true antithrombin by a reaction with heparin, and is called pro-antithrombin. It is believed that heparin and pro-antithrombin are normal constituents of circulating blood and together prevent intravascular clotting. Howell has shown that a solution of heparin has no true antithrombic action of its own but can cause a production of antithrombin when added to the blood inside or outside the body. Heparin also acts to inhibit clotting by preventing activation of prothrombin to thrombin, thus acting as an anti-prothrombin. The blood produced by the addition of heparin resembles that of hemophilia. This will be referred to later.

In the circulating blood, clotting

does not occur due to the presence of heparin and pro-antithrombin and because thromboplastin or cephalin is available in such very small amounts but when the blood is shed, circumstances are different, for then there occurs, en masse, an alteration of platelets which adds more prothrombin and cephalin to the blood, while additional amounts of the latter are also added from the tissues of the wound. The amount of cephalin is now sufficient to neutralize the effect of antithrombin and to break up combinations of prothrombin and anti-prothrombin so that coagulation commences. Even so, it appears that it is not exactly known why the initial stages of coagulation occur, though undoubtedly complex physical and chemical reactions take place, as they do in all stages of the clotting process. All investigators are agreed, however, that the reaction requires time and progresses to a definite end point.

The reaction appears to start as soon as the blood is shed. A definite amount of thrombin apparently must be formed before it is capable of reacting with fibrinogen, but when it is present in suitable amount—it converts the fibrinogen in solution in the plasma into the insoluble fibrin or clot. This process seems to be of a physicochemical nature, the fibrin being aggregated out of colloidal solution into strands.

If a drop of freshly shed blood is examined under the microscope, it will be observed after some minutes that one of the first visible changes is the drawing together of the blood platelets which then undergo a "viscous metamorphosis" whereby they fuse one with another to form hyaline elastic syncitium-like masses in which no trace of the platelet components may remain. Shortly after this fusion occurs one will observe under the microscope fine threads of fibrin and the formation of these becomes more rapid. These strands are of the nature of crystalline needles so that the clot is a crystalline jel. (Stubel & Howell—by ultramicroscope). A little while after these strands appear under the microscope, one may observe with the naked eye that the blood begins to thicken. With normal blood the process increases rapidly and the blood sets in a firm jel. Normally the clot begins to retract and to express serum shortly after coagulation is completed and continues to do so for a period of hours. The clot becomes firmer as it retracts.

It is to be recognized that blood is an extremely labile substance and that very little physical or chemical alteration in it may influence markedly the rate of coagulation and the character of the clot. One may alter the blood outside the body in some apparently insignificant way which will permit a distinctly abnormal blood to act in an apparently normal way. Thus in the determination of clotting time some few precautions must be taken. Specimens of blood for comparison must not only be obtained by the same technique but handled in precisely the same manner. The blood must be obtained directly from a vein by vein puncture and not from a small wound. The admixture of tissue juice which may occur with the blood from such wounds will accelerate coagulation, sometimes markedly. The blood should be obtained quickly and with as little trauma as possible because air, trauma, etc., will all accelerate coagulation time. Even the size and shape of the vessel into which the blood is put may have an effect. Temperature is also an important factor. Over 30° C coagulation is markedly accelerated while below 20° C coagulation is delayed. A constant temperature of about 23° C is to be preferred.

Etiology of Thrombopenic Purpuras*

The chief pathologic feature of haemorrhagic purpuras primary or symptomatic is the diminution of blood platelets. The bleeding time is greatly

*See classification at the end of this article.

increased, while the coagulation time is sometimes normal but more often slightly delayed and rarely much prolonged. The clot when coagulation takes place may be soft or firm but it fails to retract and there is no extrusion of serum.

The view is widely held that the great reduction of the platelets is the chief factor in the production of Essential Thrombopenic Purpura (Hayem, Duke and Frank). Stephan believes that damage to the endothelium of the capillaries is the primary cause. Other authors including Morawitz and Werner Schultz look upon the disease as due to changes in both the blood platelet production and in the capillaries. It seems probable that reduction in the number of platelets and injury to capillaries are coordinate phenomena.

Diminution of the platelets may be brought about in three ways:

1. Destruction or depressed activity of the megakaryocytes of the marrow, with or without similar action on the other elements of the marrow.

2. Displacement of the megakaryocytes by abnormal cells in the bone marrow.

3. Rapid destruction of the platelets in the circulation or in some organ of the body.

Let us consider these in order:

1. Destruction or depressed activity of the megakaryocytes may be caused in purpura haemorrhagica by some recognized or unrecognized toxin. This type of action has been shown to cause symptomatic haemorrhagic purpura in benzol poisoning and in ideopathic aplastic anemia. The process of aplasia may also occur in certain infections and in cases of sepsis. When aplasia or partial aplasia occurs, the megakaryocytes have been shown to vanish along with the other marrow cells.

Various toxins, for instance those of the acute infections, may poison the platelet forming centres in the marrow so that a reduced platelet count occurs in the peripheral blood. Diphtheria toxin and tuberculin as well as benzol are among the substances that have this action. Thus a symptomatic thrombopenic purpura may occur in diphtheria or tuberculosis, especially miliary tuberculosis.

It is possible that the spleen is responsible for an inhibitory agent having a specific effect on the platelet forming centres and thus depressing their activity.

2. Displacement of megakaryocytes by abnormal cells occurs in lymphatic leukemia, in which, as shown by autopsy studies, the lymphoid cells crowd out the normal platelet forming elements. The increased formation of abnormal red cells in pernicious anemia may act in a similar manner. Malignant tumors causing thrombopenia act in this way and perhaps also miliary tubercles.

3. Of destruction of platelets in the peripheral circulation there is no absolute proof. Such destruction, if it occurs, must take place fairly rapidly, since the normal life of platelets is only from 3 to 5 days.

Experiments have shown that rabbits can be immunized against guinea pig platelets and that the serum from such rabbits will cause, in dilution as high as 1 in 328, agglutination and lysis of normal guinea pig platelets while normal rabbit serum seldom causes this in dilutions greater than 1 in 6. Guinea pigs inoculated with such an anti-platelet serum develop all the features of purpura haemorrhagica and do so much more rapidly than could be accounted for by the assumption of cessation of platelet formation. Moreover the marrow of such animals shows no definite abnormalities.

During anaphylactic shock, platelets disappear from the peripheral circulation. They are not destroyed but tend to clump in the internal organs principally the spleen. If such a pro-

cess occurs in purpura haemorrhagica an explanation would be furnished for the beneficial effect of splenectomy. The improvement noted in purpura haemorrhagica after removal of the spleen may, on the other hand, be due to the removal of the source of the hypothetical agent inhibiting platelet formation. Possibly both factors contribute.

It is evident that reduction of platelets by damage to bone marrow does not occur in Essential Thrombopenic Purpura nor that their diminution can be acocunted for by true aplasia. Whether the process is comparable to an anaphylactic phenomenon or to the reaction of experimental animals inoculated with antiplatelet sera or whether it is due to a poison or inhibitory agent which acts rather specifically on the giant cells of the marrow, is not known. Possibly a combination of such processes occurs.

Why a reduction in the number of platelets in the circulating blood should be associated with a liability to haemorrhage is not understood. Pratt has suggested the possibility that the platelets have a hormone action on the capillaries. Others believe that the same agent which causes the reduction in platelets coincidently causes capillary damage.

In any case, the red cells escape in large numbers through the cement substance between the endothelial cells of the capillaries. The red corpuscles have no amoeboid activity but are flexible and capable by temporary distortion of passing through very small spaces. Arnold has suggested that they are carried through with a stream of plasma which escapes at the same time.

Capillary pressure appears to be a factor since the purpuric spots tend to appear in the dependent parts of the body. This factor is also illustrated in the production of haemorrhages into the skin of the arm by the application of a blood pressure cuff at a pressure slightly below the disastolic pressure.

Etiology of Non-thrombopenic Purpuras.

Anaphylactoid Purpura or Schonlein-Henoch disease has no relation whatever to anaphylaxis. The disease seems to be an intoxication due to histamine-like substances. Possibly it is from the intestine due to the production of toxic amino-bases from the protein of food by certain intestinal bacteria. But this is mere hypothesis. There is no evidence pointing to infection as a cause. The frequent presence of an erythemataus rash and oedema before the appearance of purpura points to a progressive capillary damage dilating them and increasing their permeability till haemorrhage finally occurs.

Poisons with a histamine-like action produce strong contraction of the smooth musculature of the intestine. This offers a possible explanation of the colic in Henoch's purpura.

Purura Simplex is no longer recognized as a disease entity. Probably many of the cases formerly included under the name were examples of mild anaphylactoid purpura.

Symptomatic Purpura may occur in the course of any infectious disease, without any alteration of the blood platelets, bleeding time or clotting mechanism. The blood will show only the changes due to the pathological condition in which the purpura occurs as a symptom. Such purpuras seem to depend entirely on capillary damage. Apparently the same mechanism which produces a rash may produce purpura by some modification, which occurs most commonly in the severe types of infection. Purpura in infections may also be produced by bacterial emboli and occurs typically in subacute endocarditis.

Intoxications. There is a long list of drugs which may produce purpura. Iodine heads the list. The iodides do not give rise to purpura except in individuals with marked idiosyncrasy. Drugs as well as unknown toxins may

perhaps produce purpura by bringing about an alteration in the inorganic metabolism of the blood, this alteration presumably permitting an increase in permeability of the capillary walls. That an alteration of the inorganic substance of the blood can produce such a change is suggested by the experiments of Chiari and Januschke. They have shown that if sodium iodide is injected intravenously in dogs, fluid escapes into the pleural and other serous cavities of the body while if calcium chloride is injected simultaneously these cavities remain dry.

Beside drugs, such toxic substances as the endotheliolysin of snake venom or histamine may excite purpura by capillary damage.

Purpuras of Endocrine and Nervous Origin.—Endocrine influences are probably concerned in the production of the purpuras associated with the menstrual function. Beyond this no one has even attempted to theorize.

There are on record well authenticated cases of purpura developing in persons of nervous temperament after severe fright; cases of severe neuralgia and muscular spasms have been reported in which purpuric spots appeared at or near the painful spots. Rarely a purpuric eruption may be seen along the courses of certain nerves. Purpura of such a nature may be only an atypical form of herpes. Unfortunately the condition of the ganglia of the posteria roots in these cases has not been ascertained.

Mechanical Causes.—Purpura from mechanical causes seems to depend on increase in capillary pressure. It may occur where venous stasis develops. It may follow paroxysms of whooping cough or an epileptic seizure. It may also be produced by the application of tight bandages or tourniquets in individuals who show no general purpurie condition.

Jaundice.—With severe liver damage fibrinogen, which is formed particularly in the liver, may become deficient, but a haemorrhagic state dependent on jaundice may occur even if fibrinogen is present in adequate amounts. Coagulation time of the blood is delayed; the bleeding time is rarely slightly prolonged. The lengthened clotting time is due largely to a lack of available calcium ions (Lee and Vincent). Though an excess of calcium usually counteracts the effect of bile on the blood, bile has an additional inhibitory effect on the formation of thrombin and in very strong concentration in vitro may prevent coagulation, even in the presence of an excess of calcium.

Etiology of Haemophilia.

Definition.—Haemophilia is an hereditary constitutional anomaly limited to the male, but transmitted by the female, characterized by a tendency to serious haemorrhage from trivial cuts and abrasions and by a marked delay in the coagulation of the blood.

According to this definition, haemophilia is a biological entity and should be considered as such. How the abnormal condition of haemophilics originated is unknown, but there is some historical evidence to show that the disease must have been known to the ancient Jews. Once the disorder is started it is transmitted through generation after generation by the female descendants, although it is only manifested in males. This is known as Nasse's law.

Cases of haemophilia have been reported from time to time in which no inheritance was demonstrated, but they are regarded as instances of the classical disease in which the ancestors, and especially the collaterals, have not been thoroughly searched for conductors or else as cases of one of the varieties of pseudo-haemophilia.

While there is still some question about the occurrence of haemophilia in the female, for the meantime, non-existence of the disease in females should be assumed.

The Blood in Haemophilia.

Careful study of the blood in typical cases have shown that the blood plate-

lets are never diminished, in fact they are somewhat increased. The fibrinogen and calcium are considered to be within normal limits. The coagulation time is prolonged but the completely formed haemophilic blood clot is as tough and firm as normal blood clot and retracts in normal fashion. The tissue juice from haemophilic organs has been shown to accelerate clotting in a normal manner.

Associated with the absolutely definite finding of prolonged coagulation time, is rather positive evidence either that one of the antecedent substances of thrombin is somewhat defective or that the cause of the defective coagulation lies in some disturbance of the formation of thrombin. It is not entirely agreed whether this deficiency is qualitative or quantitative, but the fact that thrombin when once formed is normal in amount would suggest that this deficiency is qualitative.

Minot and Lee and also Fonio, have felt that they could definitely ascribe this qualitative deficiency to one of the antecedent substances of thrombin, namely, to a defect, presumably hereditary in the blood platelets. This defect, they believe, consists of a slow availability of the platelets for the purpose of coagulation. They also noted that isolated haemophilic platelets acted very differently from isolated normal platelets in that they act very much more slowly in the formation of thrombin. These experiments are amply confirmed by clinical observation. Transfusion will bring about an alteration in haemophilic blood reducing its clotting time, this effect lasting about as long as the life of blood platelets introduced by such transfusion.

It has also been suggested that the haemophilic blood defect is due to an increase in antithrombin. The slight increase in antithrombin found in haemophilic blood can be accounted for without the assumption that it is the chief blood defect. Howell suggests that in haemophilia there may occur abnormal amounts of heparin — the anti-prothrombin substance described above. Whether or not this abnormality exists remains to be proved by methods which are not at present available to demonstrate the amount of heparin in the blood.

Fibrinopenia.

In this recently described constitutional deficiency there is a complete lack of fibrinogen in the blood and clotting is therefore impossible. The first case was reported by Rabe and Soloman in 1920. In this disease platelets are present in normal numbers. Blood withdrawn from a vein does not coagulate spontaneously nor on addition of fresh serum, tissue extracts, or normal blood platelets. No fibrinogen is demonstrable by salting or heating the plasma.

Clinical Classification.

The older classifications of purpuras divided these into primary and secondary. The primary purpuras included only purpura haemorrhagica; the remaining were classed as secondary. Obviously such a classification was most unsatisfactory since it did no more than split off one disease entity.

Modern classifications are based on the platelet count. All purpuras are divided into Thrombopenic and Non-thrombopenic. In the former group purpura haemorrhagica is given a place by itself.

The following classification is that given by Pratt and is modelled on the plan originally suggested by Leschke. It includes all the haemorrhagic diatheses.

I. **Essential Thrombopenic Purpura** (Essential Thrombopenia, Purpura Haemorrhagica, Werlhof's disease).

II. **Symptomatic Thrombopenic Purpuras.**

(a) **Blood diseases** (lymphatic leukemia, prenicious and aplastic anemia, hemolytic jaundice, carcinomatosis of the bone marrow, Hodgkin's disease, etc.).

(b) **Infections** (sepsis, subacute endocarditis, typhoid fever, etc.).

(c) **Intoxications**—(benzol, benzine, arsphenamine).

(d) **Anaphylaxis.**

(e) **Avitaminosis.**

III. **Non-thrombopenic Purpuras.**

(a) **Anaphylactoid Purpura** (Schonlein.—Henoch disease).

(b) **Purpura Simplex.**

(c) **Purpura Fulminans.**

(d) **Avitaminosis** (Scorbutus, Barlow's disease).

(e) **Capillary weakness.** (Purpura senilis, purpura cachetica, purpura of unknown etiology).

(f) **Infections** (bacterial capillary emboli or toxic capillary injury in septic diseases).

(g) **Intoxications** (iodine, benzol, arsphenamine, pyridine, snake venoms, etc.).

(h) **Endocrine and Nervous Origin.**

(i) **Mechanical Causes.**

(j) **Jaundice.**

IV. **Haemophilia.**

V. **Fibrinopenia.**

VI. **Haemorrhagic Disease of New-Born.**

Medical Athletics.

By ART WALKER, 2T9.

Medical athletics received a real boost on March 26th, when Junior Meds. basketball team won the Sifton Cup, emblematic of the interfaculty championship.

The final match, a two game series, produced some of the most brilliant basketball that has been seen in interfaculty competition for many a day. Defeated by St. Michael's in the first game by seven points, the Juniors, by a super effort, won the second contest 29-21, thereby winning the trophy by a single point.

The game, thrilling throughout, worked up to a dramatic climax in the last three minutes of play. At that time, Meds., one point down on the second game and seven points behind on the round were battling vigorously, while the Saints, struggled to protect what seemed to be a safe lead. The break came when "Spike" Sarbe made a long shot. A minute later Carss, unguarded, scored an easy basket. Now only one point down Meds., came on relentlessly. With a minute to go Sniderman scored. The cheers of the Med. supporters rocked the building. Their team needed but one point to tie the round and two to win the cup. Twenty seconds were left to play when Carss, attempting to shoot was fouled. Two free throws were awarded and Carss, coolness personified sunk the first to tie the round and scored the second, giving Meds. the Cup, for in the remaining seconds the Saints failed to score.

Every man on the Med. team played sensational basketball. Captain Jim Scott and Jimmy Sinclair were towers of strength on the defence, while Sniderman, Garbe and Carss formed a forward line with marked scoring ability. Heller, Jessyl and Kassler were able substitutes.

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EDITORIAL.

It is with regret that we are compelled to delay our resumé of the hospitals of Toronto until this Fall. We are entirely too crowded for space at present.

This will be our last opportunity editorially to make ourselves known to our readers. One may wax sentimental or with an indifferent shrug pass off the time that is growing near to those of us in the sixth year. But above all we realize this to be true, that though we soon hope to go forth as graduates, we have yet a great deal to learn—in fact we thought we knew more in the fourth year than we now know we know in the sixth. True indeed, students of Aesculapius are students for life. As we walk across the campus and hear the chimes of the Soldiers' Memorial Tower, we realize that the end is near—too near.

The past year has been a successful year for the Journal. The editorial section has come to stay, and the new arrangement of the editorials has been quite satisfactory. Next year we understand a better quality paper will be used and more careful editing be introduced—in any case we of the Journal thank the Faculty and students as well as our Alumni subscribers, for their aid and encouragement.

Fred. Kergin, B.A., 3T0, is the edi-

tor-in-chief for 1929-30, and C. G. Stogdill, B.A., M.A., 3T0, the assistant editor. Mr. Kergin edited the March number of the Journal in a highly creditable manner. Mr. Stogdill has had considerable previous experience and should fit into the next staff quite nicely. Under the editorial guidance of Mr. Kergin we look for continued success for the journal.

To exercise an Editor's prerogative a few thoughts in passing may not be amiss. The older the Journal gets naturally the more established it becomes. That it is a unique publication none will deny. However, the older constitution of the Medical Society did not take into consideration several important incidences to the yearly routine of the Journal. These are now being remedied and it is to be hoped will be heartily backed by the members of the Society when their purpose is explained to them. Another "thought" is that an even better Journal could be put out if the Faculty had an active interest in it other than the publication of articles as at present. Some even believe the Journal under complete Faculty supervision and independent of the Medical Society would be advantageous. Another point has been raised this year due to the almost 90% subscription to the Journal in each year, and that is that $1.25 should be levied on the Faculty fees for the Journal. It would no doubt give more leeway, better printing, more cuts, graphs, etc. Some of these things will eventually come to pass no doubt, others will be replaced, but be that as it may, the Journal is here to stay.

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